

AMENDMENTS TO THE CLAIMS

A listing of all currently pending claims is provided and will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of selection and/or identifying at least one ~~one or more~~ protein affinity ligands by inverse screening, wherein the affinity ligands are antibodies, that bind to at least one ~~or more~~ target proteins of interest, comprising the steps of:

- (A) obtaining a real or theoretical mass spectrometry based characterization of the at least one ~~or more~~ target proteins by either:
 - i. subjecting ~~the one or more~~ at least one target proteins to a mass spectrometry based characterization; or
 - ii. predicting the mass spectrometry based characterization from known data;
- (B) utilizing ~~the one or more~~ said at least one target proteins ~~either individually or as a mixture to:~~
 - i. generate at least one ~~one or more antibodies~~ antibody thereto by immunization; and/or
 - ii. select, using a single or multiple rounds of binding, said at least one antibody ~~one or more antibodies~~ thereto;
- (C) screening at least one antibody ~~to one or more antibodies~~ generated in step B(i) and/or ~~multiple antibodies~~ selected by step (B)(ii) by:
 - i. adding said at least one ~~a mixture of proteins or the one or more target proteins~~ individually to at least one antibody ~~the one or more antibodies~~ generated in step (B)(i) or the at least one antibody [one or more antibodies] selected in step (B)(ii),

each antibody being used individually, ~~wherein the mixture of proteins contains the one or more target proteins of interest,~~ and

ii. ~~after removing any proteins which have not bound,~~ eluting the at least one target protein that has bound;

(D) subjecting the at least one eluted target protein to mass spectrometry based characterization; and

(E) by comparing the mass spectrometry based characterization obtains in steps (A) and (D), selecting and/or identifying ~~that~~ said at least one antibody that binds to said at least one ~~the one or more target~~ protein of interest.

2. (Currently Amended) A method as claimed in claim 1 wherein the at least one ~~or more target~~ proteins of interest have been previously resolved by 2D electrophoresis.

3. (Currently Amended) A method as claimed in claims 1 or 2 wherein between steps (B) and (C) the at least one antibody ~~antibodies~~ obtained in step (B)(i.) are cloned.

4. (Currently Amended) A method as claimed in claim 1 wherein the at least one ~~or more target~~ proteins of interest are present in a mixture of proteins.

5. (Currently Amended) A method as claimed in claim 1 wherein the method is a method for selecting and identifying at least one protein affinity ligands to at least one ~~a plurality of target~~ proteins.

6. (Previously Presented) A method as claimed in claim 1 wherein the mass spectrometry based characterization further includes acquisition of sequence tag data.

7. (Currently Amended) A method as claimed in claim 1 wherein the at least one antibody ~~antibodies~~ optionally generated in step (B)(i) is ~~are~~ immobilized on a support comprising nitrocellulose or PVDF.

8. (Currently Amended) A method as claimed in claim 7 wherein the support upon which the at least one antibody is ~~antibodies are~~ immobilised and the nitrocellulose or PVDF are treated with an oligosaccharide or polyvinylpyrrolidine solution to block any remaining binding sites.

9. (Original) A method as claimed in claim 8 wherein the oligosaccharide is ficoll.

10-11. (Canceled)

12-16. (Canceled)

17. (Previously Presented) A method as claimed in claims 1, 2, 7, 8, or 9-wherein the mass spectrometry based characterization is obtained by mass spectrometry.

18. (Previously Presented) A method as claimed in claims 1, 2, 7, 8, or 9 further comprising the use automated high-throughput mass spectrometry.

19. (Currently Amended) A method as claimed in claim 2 wherein the at least one antibody ~~antibodies~~ generated in step (B)(i.) is ~~are~~ immobilized on a support comprising nitrocellulose or PVDF.

20. (Currently Amended) A method as claimed in claim 19 wherein the support upon which the at least one antibody is ~~antibodies are~~ immobilized are treated with an oligosaccharide or polyvinylpyrrolidine solution to block any remaining binding sites.

21. (Previously Presented) A method as claimed in claim 20 wherein the oligosaccharide is ficoll.

22-27. (Canceled)

28. (Currently Amended) A method as claimed in claim 2 wherein the at least one of more target proteins of interest are present in a mixture of proteins.

29. (Currently Amended) A method as claimed in claim 2 wherein the method is a method for selecting and identifying protein affinity ligands to a plurality of proteins.

30. (Previously Presented) A method as claimed in claim 2 wherein the other mass spectrometry based characterization includes acquisition of sequence tag data.

31. (Previously Presented) The method of claim 1 wherein said mass spectrometry based characterization is a peptide mass fingerprint.

37. (Previously Presented) A method as claimed in claim 1 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

38. (Previously Presented) A method as claimed in claim 37 wherein the eluting agent is formic acid.

39. (Previously Presented) A method as claimed in claim 8 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

40. (Previously Presented) A method as claimed in claim 39 wherein the eluting agent is formic acid.

41. (Previously Presented) A method as claimed in claim 19 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

42. (Previously Presented) A method as claimed in claim 41 wherein the eluting agent is formic acid.

43. (Previously Presented) A method as claimed in claim 20 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

44. (Previously Presented) A method as claimed in claim 43 wherein the eluting agent is formic acid.

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45. (Previously Presented) A method as claimed in claim 21 wherein an eluting agent is further provided for eluting protein from antibody-protein complexes.

46. (Previously Presented) A method as claimed in claim 45 wherein the eluting agent is formic acid.